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Original Research Article

Prospective Study of Clinical Features and Sequelae of Suspected Cases of Chikungunya Fever Admitted in Urban Areas of Central India

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ABSTRACT

Introduction: The fever epidemic that started in 2005-2006 in India was of re-emerging disease Chikungunya occurring after a gap of 32 years. Chikungunya fever is an arthropod-borne viral infection caused by Alphavirus and transmitted by Aedes aegypti mosquito.
Objectives of the study: This study was done to evaluate the clinical features of the suspected cases of Chikungunya fever admitted/attended in Out Patient Department (OPD) in the institution and also, to find the sequelae of joint involvement of suspected cases at the end of 6 months. Basic procedures and methodology: It is a follow-up done among the patients admitted/attended in OPD, who were more than 12 years of age with symptoms of Chikungunya and who gave their consent; attending three different hospitals were selected by systematic random sampling for the study during one year of study period. Total enumeration of all the patients was done. Suspected cases of Chikungunya fever are interviewed using a pre-tested questionnaire for data collection and were examined clinically in detail and were given treatment. Routine investigations were done in all indoor patients and selected OPD patients. Serological test for Chikungunya virus in all the suspected cases was not feasible. Hundred patients could be made available for follow up. The analysis of follow-up patients was done accordingly to know the sequelae of Chikungunya. The collected data was tabulated and analyzed using Epi-info software. Chi-squared test was used as tests of significance. P value of < 0.05 was considered significant. The ethical clearance was taken from the institution to conduct the study.
Results: Total numbers of patients were 1056 with 423 males and 633 females. The male to female ratio is 1:1.5. The maximum numbers of cases were in the age group of 20-29 yrs (25%) in which females predominate (16% with $p<0.05$).In present study it was found that headache [92.99%], backache [84.75%] and pharyngitis [88.06%] were the three main prodromal symptoms. In the present study, we found that joint affection was seen in all cases [100%].
Conclusion: In this era of travel and globalization, Chikungunya is an important differential diagnosis of febrile polyarthralgia and the health experts should empower with knowledge of control and prevention strategies to avoid its epidemic. There appears a gap in the knowledge about natural history of the disease, data on activities during inter-epidemic period, and extra human spread.
Key Words: Epidemiological investigation, Chikungunya, India

INTRODUCTION

Chikungunya fever (CHIK fever) is an arthropod-borne viral infection caused by RNA Virus Alphavirus of the family Togaviridae and transmitted by Aedes aegypti mosquito. [1] The virus, first reported

in Tanzania (1952) has been attributed to many outbreaks in a number of countries, since then. [2] Chikungunya virus is geographically distributed in Africa and Southeast Asia. [3,4] In India it was first isolated during the outbreak of haemorrhagic fever in Calcutta in 1963. [5] Followed by outbreaks in 1964 in South India (Vellore, Chennai, Puducherry) [6,7] and epidemics in central India at Nagpur (1965) and Barsi (1973). [8,9] Sporadic cases were regularly reported from the affected regions. It was a forgotten disease until recently; when it re-emerged in Indian Ocean islands in 2005-2006. It became a major health problem affecting millions of people in Asian countries, mainly India and Southeast Asian countries. [1] The decreasing trend of the epidemic has been observed over the years, despite this trend, Chikungunya remains a threat for the region and the world. It is not considered to be a fatal disease; however in 2005-2006 it caused many fatalities. [10] It is known to cause temporary disability in larger proportions due to residual joint pain (Post-Chikungunya Arthritis). [6]

Clinically, it is characterized by abrupt onset of fever with chills and headache, joint pain, and swelling especially involving small and large joints. Various types of rashes develop usually after the subsidence of fever and in the convalescent phase. [11] The rare complications include myelomeningoencephalitis, Guillain Barre Syndrome, fulminant hepatitis, myocarditis and pericarditis. [1] Acute-onset visual loss due to optic neuritis may be associated with CHIKV infection. [12] It is usually self-limiting but in some cases, symptoms may persist for months before resolution. A destructive arthropathy may occur in few adult patients with chronic symptoms. [13]

The fever epidemic which started in 2005-2006 in Central and Southern India was serologically proved to be Chikungunya by analysis carried out at National Institute of Virology (NIV), Pune. Many patients with typical features of Chikungunya reported to various hospitals in the district Aurangabad giving us the opportunity to do the present study which was undertaken to evaluate the clinical features of the suspected cases of Chikungunya fever admitted/attended in OPD in the institution and also, to find the sequelae of joint involvement of suspected cases of Chikungunya fever at the end of 6 months. As a laboratory diagnosis of every case was not feasible, this survey was based on a syndromic approach. The cases however could be linked epidemiologically to the confirmed cases of Chikungunya fever.

MATERIALS AND METHODS

Setting: The patients admitted/attended in OPD of three different hospitals were selected for the study.

Study design: Follow-up (Longitudinal study), Descriptive

Study period: The study was conducted for a period of one year with data collection done for four months (July to October 2006).

Study participants: Total enumeration of all the adult patients more than 12 years of age with symptoms of Chikungunya and who gave their consent, were included in the study.

Study tools: Pre-Designed and Pre-Tested Questionnaire was used to collect the data.

Sampling method and Sample size: All the patients who were coming to the OPD/hospital with the symptoms of Chikungunya during the study period who gave consent for the study were enrolled. Total numbers of patients were 1056 with 423 males and 633 females.

Method of data collection: Suspected cases of Chikungunya fever are interviewed on the basis of a Pre-Designed and Pre-Tested questionnaire. All the adult patients more than 12 years of age with symptoms of Chikungunya, who gave their consent, were included in the study. They were examined in detail, clinically for general and systemic examination. Routine investigations such as haemogram, urinalysis, etc were done in all indoor patients and selected OPD patients. Serological test for Chikungunya virus in

suspected cases of Chikungunya fever could not be conducted because of unavailability of commercial testing kits in the institution and samples were not being accepted at NIV, Pune probably because of large epidemic. The patients were treated with medication as per discussion with senior physician.

Follow Up: An attempt was made to contact the patients on the given address/phone number and those who attended OPD for follow up. Hundred patients could be made available for follow up. The analysis of follow-up patients was done accordingly to know the sequelae of Chikungunya such as occurrence of post-Chikungunya arthritis, acute-onset visual loss, gastro-intestinal symptoms etc.

Data analysis: The collected data was tabulated and analyzed using Epi-info software. The data were presented as frequencies and percentages. Chi- squared test was used as tests of significance. P value of < 0.05 was considered significant.

Ethical clearance: The ethical clearance was taken from the institution to conduct the study. After explaining the purpose of the study, consent was taken from all the patients who were willing to participate in the study.

RESULTS

In the present study out of the total 1056 suspected cases studied, females were 633 (59.94%) as compared to males, which were 423 (40.06%). The male to female ratio is 1:1.5. The maximum numbers of cases were in the age group of 20-29 yrs (25%) in which females predominate (16% with $p<0.05$, which is statistically significant) followed by the group 40-49 yrs (19.88%) and 30-39 yrs (19.03%). It was found that in July (34.95%) and August (30.97%) there were maximum number of cases. More than half the cases studied were from rural area (51.89%) followed by urban slum (26.51%) and urban area (21.59%). It was evident in the study findings that there was presence of conditions favourable for mosquito breeding in and around house in the form of ditches (50.75%), water drums (39.39%), open gutters (20.45%), open tanks (16.66%) and construction sites (12.21%). The common symptoms were fever, arthralgia, gastrointestinal tract symptoms and ocular symptoms. Further, it was seen that all cases were having intermittent type of fever and it was associated with chills in all and rigors were also associated with in 242 (23%) of cases.

Table No.1 : Showing the frequency of involvement of different joints.

Sr. No.	Type of joint involved	No. of cases with joint affected	Percentage (n=1056)
1.	Interphalangeal joint	1011	95.73
2.	Wrist joint	1010	95.64
3.	Knee joint	1000	94.69
4.	Ankle joint	998	94.50
5.	Spine	895	84.75
6.	Metacarpo-phalangeal joint	679	64.29
7.	Shoulder joint	534	50.56
8.	Elbow	507	48.01
9.	Hip joint	331	31.34
10.	Metatarso-phalangeal joint	320	30.30

Table No. 2: Showing frequency of gastrointestinal symptoms amongst 1056 suspected cases.

Symptom	No. of cases affected	Percentage
Anorexia	493	46.68%
Vomiting	367	34.75%
Abdominal pain	206	19.50%
Loose motion	159	15.05%
Constipation	81	07.67%

Table 1 is showing the frequency of involvement of different joints. In most of the patients, the joints involved were multiple. However, the joints which showed acute signs of inflammation were taken for analysis. From this table it was clear that the joint affection was seen in all cases (100%). Table 2 shows the frequency of gastrointestinal symptoms amongst 1056 suspected cases, it is evident that the most frequent gastrointestinal symptom was anorexia (46.68%) followed by vomiting (34.75%). Table 3 shows occurrence of other symptoms amongst 1056 suspected

cases, it is evident from this table that headache was the most frequent prodromal symptom in 92.99% of cases followed by pharyngitis in 88.06%. Table 4 shows occurrence of ocular symptoms amongst 1056 suspected cases and it was evident that most frequent ocular complaint was conjunctival congestion (22.63%) followed by retro orbital pain (11.64%) and photophobia (11.36%).In the present study hemorrhagic manifestations or cardiac or respiratory complication or organomegaly on per abdominal examination were seen in none. We found that two patients had central nervous system (CNS) involvement; both of them had history of altered sensorium within 2 days of onset of fever. On examination they were drowsy; none had sign of meningitis or focal neurological deficit. All of them recovered in 2 days after onset of altered sensorium.

Table No. 3: Showing occurrence of other symptoms amongst 1056 suspected cases.

Symptom	Number	Percentage (%)
Headache	982	92.99%
Pharyngitis	930	88.06%
Backache	869	82.29%
Malaise	493	46.68%
Generalized itching	259	24.6%
Edema feet	207	19.60
Rhinitis	102	09.65%
Papular rash	07	0.66%

Table No. 4: Showing occurrence of ocular symptoms amongst 1056 suspected cases.

Symptom	Number	Percentage (%)
Conjunctival congestion	239	22.63%
Retro orbital pain	123	11.64%
Photophobia	120	11.36%

Table No. 5 : Showing frequency of arthralgias on follow up visits

Type of joint affected	Number of affected patients (n=100)			
	At start of study	After 1 month	After 3 months	After 6 months
Knee	n= 93 (93%) (M -39;F-54)	n=19 (19%) (M-9;F-10)	n=15 (15%) (M-8; F-7)	n=08 (8%) (M-5; F-3)
Ankle	n= 91 (91%) (M-42; F-49)	n=22(22%) (M6;F16)	n=18 (18%) (M-5; F-13)	n=12 (12%) (M-5; F-7)
Hip	n= 33 (33%) (M-15; F-18)	NIL	NIL	NIL
Shoulder	n=49 (49%) (M-21; F-28)	NIL	NIL	NIL
Elbow	n=41 (41%) (M-20; F-21)	n=03 (3%) (M-2;F-1)	n=03 (3%) (M-2;F-1)	n= 03 (3%) (M-2; F-1)
Wrist	n=90 (90%) (M-39; F-51)	n=18 (18%) (M-2;F-16)	n=14 (14%) (M-2; F-12)	n=09 (9%) (M-2; F-7)
Spine	n= 80 (80%) (M-36; F-44)	n=08 (8%) (M-2;F-6)	n=04 (4%) (M-1; F-3)	n=01 (1%) (M-0; F-1)
IPJ	n= 91 (91%) (M-40; F-51)	n=02 (2%) (M-1;F-1)	n=02 (2%) (M-1; F-1)	n=01 (1%) (M-1; F-0)
MCP	n=45 (45%) (M-23;F-22)	NIL	NIL	NIL
MTP	n=28 (28%) (M-13; F-15)	NIL	NIL	NIL

In present study, deranged kidney function test [Blood urea 40-150 mg% and creatinine 1.5 -6 mg%] seen in 4 cases and 3 of them of them were of age > 50 yrs and 1 was of 40 yrs. Electrolyte imbalance [hyponatremia] seen in 5 cases all had age >50 yrs and had dehydration because of vomiting/loose motions. Liver function test was deranged in 2, urine routine and microscopy was normal in all.CSF examination was done in one suspected case of encephalitis, CSF proteins was 63.1 mg%, sugar 127 mg% [BSL- 150 mg%], chloride 131.4 mmol/L and cytological examination show occasional lymphocyte.

We found on follow up of the cases, at the start of study (n=100) that knee joint was seen maximally involved (93%) followed by ankle and interphalangeal joint (91%), wrist joint (90%), spine (80%), shoulder (49%), meta-carpophalangeal joint (45%), elbow joint (41%), hip joint(33%) and metatarsophalangeal joint (28%). It was evident that, patients of age <19 years had no residual joint involvement at the end of one month. The joint with maximum residual involvement was ankle (24.2%) followed by knee (20.6%), wrist (20%) and least being the interphalangeal joint (2.2%). Whereas hip, shoulder, meta-

carpophalangeal and metatarsophalangeal joint involvement was seen in none of the follow up cases (Table 5).

It is evident that at the end of 3 months, patient of age group <19 years, males between 20-29 years and 30-39 years had no residual joint involvement. The joint with maximum involvement was ankle (19.7%) followed by knee joint (16.3%), whereas hip, shoulder, meta-carpophalangeal and metatarsophalangeal joint involvement was seen in none of the follow up patients. It is evident that at the end of 6 months, patient of age <19 years, 20-29 years, males between 30-39 years and 40-49 years had no residual joint involvement. The joint with maximum joint involvement was ankle joint (13.2%) followed by wrist joint (10%), knee joint (8.7%).

DISCUSSION

During the period of July to October 2006, 1056 patients suspected to have Chikungunya were included in the study. There were 423 males and 633 females. In present study it was found that headache [92.99%], backache [84.75%] and pharyngitis [88.06%] were the three main prodromal symptoms. In a study done by Nimmannitya et al (1969) shows pharyngitis [90.3%], headache [68.4%] and nausea/vomiting [59.4%] as the major prodromal symptoms with which the patients presented. [14] The study by Rampal et al (2006) [15] shows malaise, backache and gastrointestinal symptoms in all cases; whereas the study by Borgherini et al (2005-6) [16] shows gastrointestinal symptoms in 47.1% cases.

In the present study, we found that joint affection was seen in all cases [100%]. The joint that was maximally affected was interphalangeal joint in 1011 [95.73%] followed by wrist joint in 1010 [95.64%] in upper limbs and in lower limbs knee joint in 1000 [94.69%] followed by ankle joint in 998 [94.50%]. In another study done by Nimmannitya et al (1969) [14] reported arthritis in 40% cases; Ganu A.S. (1996) [17] reported arthralgia in 100% cases; Borgherini et al (2005-6) [16] shows polyarthralgia in 96.1% cases; Rampal et al (2006) [15] show the joint involved in order of severity and preference were knee, ankle, wrist, small joints of hand and feet and elbow; Mohan (2006) [18] reported polyarthralgia in 98% of cases and George et al (2007) [19] on 100 cases show joint pain in 95% cases. Among the clinical features recorded in multi-centric study done by Ray P et al in 2012 showed that joint pain (62.8%) and headache (63.3%) were most frequently observed while other features included abdominal pain (48.1%), vomiting (43.9%) and rash (36.1%). [20]

Symptom such as lymphadenopathy was rarely observed; whereas hepatomegaly, splenomegaly, hemorrhagic manifestations, cardiac complication and respiratory complication were not observed in the present study. Lymphadenopathy was seen in 31 patients [0.029%] in the present study; all had tender-firm-mobile posterior cervical lymph nodes, whereas the study by Nimmannitya et al (1969) shows lymphadenopathy in 30.8% cases. [14] The study by Thriruvengadam et al (1964) [6] shows haemorrhagic manifestations in 11.6% cases whereas study by Nimmannitya et al (1969). [14] Ganu A.S. (1996) [17]and Rampal et al (2006) [15] reported haemorrhagic features in none of the cases however study by Borgherini et al (2005-6) [16] shows haemorrhagic manifestations are rare. The study by Nimmannitya et al (1969) [14] reported splenomegaly in 3.1% cases and cardiac or respiratory complication seen in none. The study by Ganu A.S. (1996) [17] reported renal involvement in 3% [6] of cases in form of asymptomatic urinary abnormality in 4/6, acute glomerulonephritis and acute renal failure in one out of 6 cases each. The study by Rampal et al (2006) [15] shows hepatosplenomegaly in 10% cases. Cardiac or respiratory complication seen in none.

In present study it was seen that central nervous system (CNS) involvement was present in 2 patients. Both of them had

history of altered sensorium within 2 days of onset of fever. On examination they were drowsy, with no sign of meningitis or focal neurological deficit. They recovered in 2 days after onset of altered sensorium. The study by Thriruvengadam et al (1964) [6] shows neurological manifestations in 2.06 %. The study by Ganu A.S. (1996) [17] reported nervous system involvement in 4% [8] cases in form of encephalitis, convulsion and peripheral neuropathy cases. The study by Rampal et al (2006) [15] shows occurrence of neurological symptoms and signs in Chikungunya cases (100%) were observed early in the course of disease on 2nd or 3rd day of fever. All the cases had shown altered level of consciousness in form of confusion, disorientation, drowsiness and delirium.

In present study investigation done in the patients shows, platelet count done in 108 cases, thrombocytopenia [<150000/cumm] seen in 48 cases [44%] and all of them had count 50000-150000/cumm [100%]; were as deranged kidney function test [Blood urea 40-150 mg% and creatinine 1.5 -6 mg%] seen in 4 cases and liver function test was deranged in 2 patients, urine routine and microscopy was normal in all. In the study done by Borgherini et al (2005-06) [16] shows Leucopenia as prominent finding and severe thrombocytopenia as rare to occur. In present study it was found that electrocardiogram (ECG) was done in 168 cases none of them show sign of myocarditis. The study by Thriruvengadam et al (1964) [6] shows signs of myocarditis in 09.09% cases.

In present study, CSF examination was done in one suspected case of encephalitis, CSF proteins was 63.1 mg%, sugar 127 mg% [BSL- 150 mg%], chloride 131.4 mmol/L and cytological examination show occasional lymphocyte. The study by Ganu A.S. (1996) [17] reported lymphocytic pleocytosis, mildly raised proteins on C.S.F. examination. The study by Rampal et al (2006) shows CT scan head in 10% cases had shown multiple small hemorrhages with diffuse cerebral edema in one case and ring-enhancing lesion in left basal ganglia region in other case. CSF analysis revealed raised protein (50-112 mg/dl) in 85% cases. There is no specific correlation between neurological findings and CSF abnormality.

In the present study follow up of 100 patients out of 1056 cases was done. 100 patients could be followed up on OPD basis. They were examined clinically and their laboratory investigations like X-Ray of affected joint, liver function test, kidney function test, complete blood count and peripheral smear were done after interval of one month, 3 month, 6 month from their time of discharge. None of the cases showed abnormal investigations.

The follow up of 100 cases revealed that at the end of 6 months, the joint pain in all the joints was reduced to a marked extent. This may be attributed to constant use of these joints with movements. None of the patients after 1 month follow up needed analgesic treatment. They were instructed to follow regular mild to moderate exercise at the joint. They were assured that they may have mild arthralgia for even longer period but they will not have any deformity or loss of joint movements. Study by Ganu A.S. (1996) [17] on 62 cases of persistent arthralgia [arthralgia of > one month of duration] reported, 78% of cases are of >50 yrs of age, male to female ratio was 28:36 i.e. 0.777 to 1. Knee was the most common joint to get involved in 88% cases followed by ankle in 70%, wrist in 35% cases, small joints of hand in 25% and other joints in none of cases. Risk factors for development of persistent arthralgia was age >50 years and previous arthropathy. No death was reported during this study period.

CONCLUSION

Chikungunya fever is a re-emerging disease in Indian Ocean region. The current outbreak has occurred after a gap of 32 years. The clinical features and number of people affected by this outbreak suggest of this virus is becoming more pathogenic. In this era of travel and globalization,

Chikungunya should be considered as the differential diagnosis of febrile polyarthralgia with an abrupt onset. There appears a wide gap in the knowledge about natural history of the disease, data on activities during inter-epidemic period, and possible extra human spread. The Public Health Experts should be empowered with appropriate knowledge for control, prevention strategies and formulate evidence-based outbreak management plans to avoid an epidemic of this re-emerging disease. In the light of findings of present study and other studies, it is suggested that we should develop and maintain the capacity to detect and confirm cases, strengthen our reporting system, manage patients and implement social communication strategies to reduce the presence of the mosquito vectors; and that the patients who are registered as Chikungunya should be followed for longer period to know if they develop any joint deformity or complications.

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